# *Information*

# Use of Anti-Arrhythmic Agents Other Than Digitalis

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*Material Supplied by the California Heart Association*

***Quinidine.*** The current therapeutic status of quinidine has changed little since Wenckebach's classic observations on recurrent atrial fibrillation. Although many antiarrhythmic agents have appeared on the pharmacologic horizon, none has surpassed the efficacy of quinidine, an agent effective in any active arrhythmia, whether atrial, A-V nodal or ventricular. The introduction of precordial electroshock therapy by Zoll and his associates and Lown has imparted a new dimension in the approach to antiarrhythmic therapy and made it possible to convert almost 90 percent of the patients with atrial fibrillation to sinus rhythm. Nevertheless, the usefulness of quinidine has not diminished because a pharmacologic program must be instituted to maintain a sinus rhythm even after electroconversion.

The usual drug method of converting atrial fibrillation to sinus rhythm in the digitalized patient is to administer quinidine in a dosage of 0.2 gm every two hours for five doses the first day; 0.3 gm every two hours for five doses the second day; 0.4 gm every two hours for five doses the third day; and so forth. If conversion fails at 0.6 gm (total daily dose of 3.0), the likelihood of conversion is small and the maintenance of sinus rhythm is probably not feasible. Higher doses are attended with toxicity, quinidine syncope, and cardiac standstill. Although quinidine may be useful in converting atrial flutter, the drug should not be used to convert atrial flutter with 2:1 A-V conduction ratio without previous digitalization, since the vagolytic effects of quinidine may allow 1:1 A-V conduction to occur with a dangerously rapid ventricular rate. Quinidine may be administered in a dose of 0.2 to 0.4 gm three to four times a day to control ventricular or atrial premature systoles. Quinidine may be effective in the treatment of arrhythmias associated with Wolff-Parkinson-White syndrome and occasionally it may abolish the electrocardiographic changes of this syndrome. The combination of a small dose of quinidine 100 to 200 mg four times a day with propranolol 10 to 20 mg four times a day has proved extremely effective in controlling Wolff-Parkinson-White tachycardia, recurrent atrial flutter or fibrillation and in the presence of intermittent ventricular tachycardia.

Although it has been traditionally recommended that a test of quinidine be given to elicit idiosyncrasy, many clinicians utilize the first dose of a therapeutic program for this purpose.

Toxicity may be manifested by pulmonary, gastrointestinal, or cardiac signs and symptoms. Cyanosis, respiratory depression, vascular collapse, restlessness, pallor, cold sweat and syncope are not uncommon. Cinchonism may develop, with tinnitus, vertigo, visual disturbances, headache, confusion, angioneurotic edema, nausea, vomiting, diarrhea, fever or cutaneous manifestations. Thrombocytopenia has been observed occasionally and may be associated with a grave prognosis.

A widening of the QRS complex of more than 25 percent is a warning of impending toxicity and the drug should be discontinued. Cardiotoxicity may be successfully antagonized by 40 to 80 mEq molar sodium bicarbonate or 1 to 3 micrograms per minute of isoproterenol.

***Procainamide.*** More than 40 years ago, it was found that procaine could paralyze extracardiac nerves; but, because of rapid hydrolysis, therapeutic levels were difficult to maintain and it never became a clinically useful antiarrhythmic drug. On the other hand, procainamide which binds para-aminobenzoic acid and diethylaminoethanol through an NH group is not affected by the choline esterase of the body and consequently is effective by the oral and parenteral routes with a more prolonged duration of action.

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The hemodynamic effects of procainamide are not unlike quinidine. However, large doses of intravenous procainamide may cause serious hemodynamic derangements.

Although it was originally thought that procainamide depressed contractility of cardiac muscle less than quinidine, more recent studies suggest that equivalent doses expressed as milligrams per kilogram depress cardiac muscle equally.

As in the use of quinidine, it is important to realize that patients with renal damage or with congestive heart failure excrete procainamide more slowly than do normal persons, and cumulative effects are a potential danger. Procainamide, like quinidine, acts on the atrium and ventricle by increasing the refractory period and conduction time and has anticholinergic effects on the atria and A-V node. The electrophysiologic effects of the drug are similar to those of quinidine. However, these similarities do not adequately explain the successful use of one drug when the other has failed as an antiarrhythmic agent.

Although procainamide is probably less successful than quinidine in reverting atrial fibrillation to sinus rhythm, it has been used in quinidine-sensitive patients. Likewise, it has been effective in restoring sinus rhythm in patients with atrial flutter and atrial tachycardia. Procainamide appears to have a distinct advantage over quinidine in the management of ventricular tachycardia, when urgent intravenous therapy is required. The rate of intravenous administration should not exceed 100 mg per minute, and electrocardiographic monitoring is imperative during the period of injection. We have frequently and successfully treated atrial tachycardia with block and ventricular tachycardia, with procainamide in the presence of digitalis overdosage. However, the management of ventricular or junctional tachycardia in high grade A-V block requires special attention. Depressant agents, such as quinidine, procainamide and potassium salts may abolish all subsidiary pacemakers and engender cardiac standstill. Hence, electrical pacing or isoproterenol are best utilized in this clinical setting.

The toxic signs of procainamide include hypersensitivity reactions such as skin eruptions, bone marrow depression or lupus erythematosus with proteinuria and polyserositis. The development of hypotension or widening of the QRS complex beyond 25 percent of control is a definite indication to withdraw this agent. As in the use of quinidine, infusion of hypertonic sodium salts will reverse procainamide toxicity.

***Lidocaine.*** The pharmacologic activity and electrophysiologic mechanisms of lidocaine are similar to those of quinidine and procainamide. It has proved extremely effective in terminating ventricular tachycardia, especially in the presence of an acute myocardial infarction and premature ventricular systoles.

The main hallmark of this agent is its superiority to procainamide in certain specific situations when a short-acting agent is required, particularly in hearts previously depressed by other antiarrhythmic agents or where only a transitory antiarrhythmic effect is indicated. It has been used successfully in depressed hearts following open heart surgery to control ventricular tachycardia before the termination of extracorporeal circulation. However, it is impractical for the very long term treatment or prevention of paroxysmal ventricular tachycardia. It is safe and effective in a single intravenous dose of 1 mg per kilogram with repeated doses every 20 minutes to a maximum of 750 mg. Usually a bolus injection of 50 to 100 mg is administered intravenously, followed by an intravenous drip of 2 to 4 mg per minute to prevent the reappearance of ventricular premature systoles. This agent has significantly reduced the mortality associated with ventricular tachycardia and fibrillation in the presence of an acute myocardial infarction and has become the most useful antiarrhythmic agent in the coronary care unit. Similar restrictions as stated under quinidine and procaine should be observed in the presence of high grade A-V block.

***Diphenylhydantoin.*** Diphenylhydantoin (Dilantin®) appears equally effective in both supraventricular and ventricular arrhythmias and possesses properties which make it effective against digitalis-induced arrhythmias. It has been successful in preventing paroxysmal atrial tachycardia (PAT) when the usually employed antiarrhythmic agents have failed. It has proved effective in suppressing atrial, A-V nodal, and ventricular premature systoles, and is particularly effective in terminating digitalis-induced arrhythmias. Its transient action and rapid reversibility of toxic effects may give it certain advantages over other depressant agents. However, it does not appear effective in converting atrial fibrillation to sinus rhythm. In the treatment of rapid supraventricular or ventricular tachycardias, 5 to 10 mg per kilogram can be slowly injected intravenously over a 15-minute

period and repeated within two to three hours. The drug can be administered orally, from 100 to 200 mg four times daily, for the suppression of ectopic beats or prophylaxis against recurrent paroxysmal tachycardia.

Toxic manifestations of diphenylhydantoin are seen in approximately 10 to 15 percent of patients and include nervousness, ataxia, tremors, nystagmus, visual disturbances, respiratory arrest, confusion or drowsiness, gastric distress, erythematous or morbilliform cutaneous eruptions and hyperplasia of the gums.

***Beta Adrenergic Blocking Agents.*** Interest in blocking the effects of adrenergic nerve stimuli is attributed to Dale who, in 1906, described the reversal of the pressor response to epinephrine by pretreating experimental animals with certain ergot compounds. Ahlquist recognized two types of adrenergic receptors and designated these alpha and beta.

Propranolol reduces the heart rate and cardiac contractile force. Arterial pressure and ascending aortic flow are slightly reduced in anesthetized dogs. As these changes do not occur after depletion of norepinephrine stores by syrosingopine, it is concluded that they result from blockade of resting sympathetic drive. In humans, administration of propranolol will cause a decrease in cardiac output and left ventricular work at rest and during exercise. Propranolol will abolish the vasodilation effects of epinephrine and isoproterenol but not the vasoconstrictor effects of the catecholamines on the peripheral vessels.

With intravenous administration, propranolol exerts a rapid antiarrhythmic action. Propranolol is usually given slowly in doses of 1 to 5 mg intravenously (no more than 1 mg every two or three minutes) or 15 to 30 mg three to four times daily may be given by the oral route prophylactically to prevent the return of ectopic beating. The action is usually immediate during the intravenous administration and the drug may be repeated within two to three hours.

The side effects of propranolol may include lightheadedness, drowsiness, nausea, diarrhea, sleeplessness, rashes, visual disturbances, purpura, paresthesias, flushing, and mental confusion. The pharmacologic effects of propranolol have produced hypotension, bradycardia, cardiac failure, A-V heart block, bronchial wheezing and aggravation of mild obstructive pulmonary disease.

# Current Status of Multiphasic Screening

CMA HOUSE OF DELEGATES, Resolution No. 37-69 calls for the profession to be kept informed of progress and development in the field of multiphasic screening. It also asks that appropriate component parts of multiphasic screening be defined. Since the adoption of this resolution, the need for information has increased. Multiphasic screening has become big business with major organizations promoting programs for hospitals, medical societies, union groups, retirement communities, etc. The CMA Council has given the responsibility for following developments in this field to the Commission on Community Health Services. The following is the commission's report as of this time.

Unfortunately it is not yet clear just what part multiphasic screening should properly play in health care. Nor is it possible to delineate the appropriate components of a multiphasic screening program with any precision. Therefore, this report can only raise some of the critical questions which we feel must be answered.

Programs for large populations are being promoted on the basis that they will provide early detection and/or prevention of disease. Certainly the objective cannot be questioned. However, there is little concrete evidence that the method accomplishes the objective. A large group is surveyed and the proponents report that 40 percent have been found to have positive findings. Evaluation of the significance of such positive findings must be critically examined. There is virtually no meaning in merely reporting that so many cases of a given condition were discovered as the result of a mass survey of so many people, unless it can also be demonstrated that the existence of the condition was unknown either to the patient or to his physician. Furthermore, unless it can be shown that detection of the condition materially affects the prognosis there is little value in detection per se.